UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,045	02/21/2007	Kouji Matsushima	14875-157US1 C1-A0308P-US	9112

26161 7590 06/28/2010
FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
SKELDING, ZACHARY S	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/574,045	MATSUSHIMA ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,6,8-10,14 and 21-48* is/are pending in the application.

4a) Of the above claim(s) *6,8-10,25,27,32,33,36,37,40,42,45 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,14,21-24,26,28-31,34,35,38,39,41,43,44,46 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-20-10 7-23-07 8-17-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of the species of NK inhibitor receptor of "SEQ ID NO: 4" in the reply filed on April 13, 2010 is acknowledged. The traversal is on the ground(s) that SEQ ID NOs: 2 and 4 have a common structure across much of their sequence and that because no documents have been cited anticipating this structure they share a special technical feature. This is not found persuasive because as put forth below the shared portion of SEQ ID NOs: 2 and 4 is anticipated by the prior art.

   The requirement is still deemed proper and is therefore made FINAL.

   Claims 2, 6, 8-10, 14 and 21-48 are pending.

   Claims 2, 14, 21-24, 26, 28-31, 34, 35, 38, 39, 41, 43, 44, 46 and 48 are under examination wherein the elected species of polypeptide is "SEQ ID NO: 4".

   Claims 6, 8-10, 25, 27, 32, 33, 36, 37, 40, 42, 45, and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group or species of invention there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on January 7, 2010 and April 13, 2010.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

   > A person shall be entitled to a patent unless –
   >
   > (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
   >
   > (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 2, 21-23, 26, 28, 29, 30, 38, 39, 41, 43, 44, 46 and 48 are rejected under 35 U.S.C. 102 (a/e) as anticipated by Davis et al. (WO 03/089624, cited on an IDS) or Davis et al. (7,317,087, cited on an IDS), respectively, each as evidenced by the teachings of the instant specification at page 3, 1st and 2nd paragraphs and Example 17 at pages 54-55.

   As a preliminary matter it is pointed out that the application issuing as the '087 patent was the U.S. National Stage entry of Davis et al. (WO 03/089624). While this rejection is applied under both 35 U.S.C. 102 (a) and (e) the description of the prior art teachings will refer to the text of the '087 patent.

Davis teaches the human FcRH 6 protein (SEQ ID NO: 28 of Davis) which is identical to residues 23-441 of SEQ ID NO: 4. (see attached alignment #1). Davis further teaches in one embodiment the SEQ ID NO: 28 FcRH 6 protein can have the MLLWTAVLLFVPCVG signal sequence (SEQ ID NO: 32 of Davis, see col. 8, 1st paragraph; col. 10-11 bridging and SEQ ID NO: 40 which is the polynucleotide sequence encoding residues 6-441 of claimed SEQ ID NO: 4, see attached alignment #2).

Thus, Davis teaches a polypeptide comprising SEQ ID NO: 32 (signal sequence) + SEQ ID NO: 28 (polypeptide sans signal sequence), which yields a polypeptide identical to residues 6-441 of claimed SEQ ID NO: 4. Davis also teaches fragments comprising at least 10 amino acids of the FcRH 6 protein, and further teaches that antibodies can be made that are specific for a FcRH 6 fragment (col. 8, 1st paragraph; col. 8-9 bridging; cols. 23-24).

As to claims reciting "ITIM signaling activity is a tyrosine kinase activity," while Davis teaches that the polypeptide encoded by SEQ ID NO: 40 has "a single or two ITIM's," (see col. 36), Davis does not demonstrate that the sequence has ITIM signaling activity. However, as evidenced by the teachings of the instant specification at page 3, 1st and 2nd paragraphs and Example 17 at pages 54-55, when the intracellular portion of SEQ ID NO: 4 is linked to the extracellular portion of CD8, the resulting chimera expressed in a cell containing a reporter for ITIM activity, and the CD8 extracellular domain crosslinked with anti-CD8 antibody, the chimera has ITIM signaling activity. Given the extensive identity between the SEQ ID NO: 4 and the polypeptide encoded by SEQ ID NO: 40 of Davis, and further given that as is well known in the art N-terminal signal sequences are cleaved upon translocation into the ER, the polypeptide of Davis, like claimed SEQ ID NO: 4, necessarily possesses the ability to mediate ITIM signaling.

Since the Office does not have a laboratory to test the reference polypeptides for ITIM tyrosine kinase signaling activity it is applicant's burden to show that the reference polypeptides do not possess this activity. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Applicant is reminded in this regard that "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)." See MPEP § 2112.01.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 14, 21-24, 26, 28-31, 34, 35, 38, 39, 41, 43, 44, 46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (WO 03/089624) or Davis et al. (7,317,087), respectively, in view of Takao et al. (JP 2004-208583, published July 29, 2004, cited on an IDS) as evidenced by the teachings of the instant specification at page 3, 1st and 2nd paragraphs and Example 17 at pages 54-55 and the Japanese language Machine translation of Takao et al. JP 2004-208583, translated June 18, 2010, pages 1-32, cited herewith).

Davis teaches the human FcRH 6 protein (SEQ ID NO: 28 of Davis) which is identical to residues 23-441 of SEQ ID NO: 4. (see attached alignment #1). Davis further teaches in one embodiment the SEQ ID NO: 28 FcRH 6 protein can have the MLLWTAVLLFVPCVG signal sequence (SEQ ID NO: 32 of Davis, see col. 8, 1st paragraph; col. 10-11 bridging and SEQ ID NO: 40 which is the polynucleotide sequence encoding residues 6-441 of claimed SEQ ID NO: 4, see attached alignment #2).

Thus, Davis teaches a polypeptide comprising SEQ ID NO: 32 (signal sequence) + SEQ ID NO: 28 (polypeptide sans signal sequence), which yields a polypeptide identical to residues 6-441 of claimed SEQ ID NO: 4. Davis also teaches fragments comprising at least 10 amino acids of the FcRH 6 protein, and further teaches that antibodies can be made that are specific for a FcRH 6 fragment (col. 8, 1st paragraph; col. 8-9 bridging; cols. 23-24).

However, Davis does not teach the N-terminal 7 amino acids of SEQ ID NO: 4. Moreover, Davis does not teach a kit comprising the polypeptide of SEQ ID NO: 4 with fifty or fewer substitutions, deletions or insertions wherein the polypeptide has ITIM signaling activity.

That said, Takao teaches the human MCD055 protein (SEQ ID NO: 2 of Takao) which is identical to residues 1-400 of SEQ ID NO: 4 (see attached alignment #3). Takao further teaches the full length polynucleotide encoding the MCD055 protein, SEQ ID NO: 3, which as would be obvious to one of ordinary skill in the art from the attached alignment #4 has some differences at the 3' end that cause a frameshift relative to a polynucleotide that encodes the mature form of Davis FcR H6.

With respect to the MCD055 signal sequence Takao teaches the following: "In the protein which has a signal sequence, that from which the signal sequence was cut may be functioning as a maturation protein. Therefore, if the mature peptide in which the signal sequence was removed from the protein of this invention is also a substance equivalent to this invention substantially, he should understand it. In the case of MCD055, existence of a signal sequence is predicted 24th near [the 2nd to] the amino acid residue of the amino acid sequence shown in SEQ ID NO 2 (when film penetration prediction program SOSUI is

used). Although the range of a signal peptide field may produce some difference by a prediction program and diversity may arise in how a signal peptide is removed also in the protein produced experimentally, As long as it is functionally equivalent as MCD055 protein, it should be understood that it is a substance equivalent to this invention." (see Section [0033] of the Japanese language machine translation cited herewith).

It would have been obvious to one of ordinary skill in the art considering the disclosed nucleotide sequences of Takao and Davis (see SEQ ID NOs: 3 and 40, respectively), that the polypeptide of Davis may be modified by using the signal sequence of Takao which represents a 7 amino acid N-terminal extension of the FcR H6 signal sequence disclosed by Davis. Given that Takao and Davis each teach that their disclosed signal sequence is suitable for directing the secretion of MCD055 and FcR H6, respectively, one of ordinary skill in the art would have had a reasonable expectation of using the signal sequence of Takao as in obvious alternative to that of Davis.

As to the claimed Kit, it would have been obvious to one of ordinary skill in the art to make a kit comprising the polypeptide of SEQ ID NO: 4 with fifty or fewer substitutions, deletions or insertions wherein the polypeptide has ITIM signaling activity, such as a kit comprising Davis SEQ ID NO: 28. One of ordinary skill in the art would have been motivated to do so because it would be useful to identify a potential ligand for Davis SEQ ID NO: 28, such as an antibody that binds Davis SEQ ID NO: 28 so as to further investigate the expression of SEQ ID NO: 28 in various tissues.

In conclusion, given the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

As to claims reciting "ITIM signaling activity is a tyrosine kinase activity," while Davis teaches that the polypeptide encoded by SEQ ID NO: 40 has "a single or two ITIM's," (see col. 36), Davis does not demonstrate that the sequence has ITIM signaling activity. However, as evidenced by the teachings of the instant specification at page 3, 1st and 2nd paragraphs and Example 17 at pages 54-55, when the intracellular portion of SEQ ID NO: 4 is linked to the extracellular portion of CD8, the resulting chimera expressed in a cell containing a reporter for ITIM activity, and the CD8 extracellular domain crosslinked with anti-CD8 antibody, the chimera has ITIM signaling activity. Given the extensive identity between the SEQ ID NO: 4 and the polypeptide encoded by SEQ ID NO: 40 of Davis, and further given that as is well known in the art N-terminal signal sequences are cleaved upon translocation into the ER, the polypeptide of Davis, like claimed SEQ ID NO: 4, necessarily possesses the ability to mediate ITIM signaling.

Since the Office does not have a laboratory to test the reference polypeptides for ITIM tyrosine kinase signaling activity it is applicant's burden to show that the reference

polypeptides do not possess this activity. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Applicant is reminded in this regard that "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)." See MPEP § 2112.01.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 14, 21-24, 26, 28-30, 43, 44, 46 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims encompass in their breadth variants of SEQ ID NO: 4 that have ITIM signaling activity.

The knowledge in the art of making modified versions of SEQ ID NO: 4 that retain ITIM signaling activity is low.

The instant specification discloses SEQ ID NO: 4 is expressed in mature NK cells, that it has homology to NKIR polypeptides and that it has two putative ITIM motifs which are commonly found in NKIRs. Therefore the instant specification concludes SEQ ID NO: 4 is a NKIR capable of recognizing, "as a ligand, classic MHC class I belonging to the FcR superfamily" (see pages 3-4 and 36, last paragraph to page 37 1st paragraph).

Moreover, Example 17 at pages 54-55 of the instant specification shows that when the intracellular portion of SEQ ID NO: 4 is linked to the extracellular portion of CD8, the resulting chimera expressed in a cell containing a reporter for ITIM activity, and the CD8 extracellular domain crosslinked with anti-CD8 antibody, the chimera has ITIM signaling activity.

Neither the teachings of the instant specification nor the knowledge in the art are sufficient to make the genus of polypeptides claimed.

While example 17 of the instant specification provides an assay that could be used to look for variants of a CD8 extracellular domain/SEQ ID NO: 4 intracellular domain chimera that have ITIM signaling activity, it does not provide the skilled artisan with an assay that can be used to look for genus of SEQ ID NO: 4 variants, i.e., including variations in the extracellular region of SEQ ID NO: 4, that have ITIM signaling activity. The issue is the instant specification does not teach which particular classical MHC class I molecule is capable of binding and activity the ITIM signaling activity of SEQ ID NO:4. Moreover. determining if a given NKIR recognizes and is activated by a particular classical MHC class I is often yields inconclusive results (see Long et al., Semin Immunol. 2000 Apr;12(2):101-8, page 104, left col., cited herewith). In the absence of an identified ligand capable of activating the ITIM signaling activity of SEQ ID NO: 4 it is unclear how the skilled artisan is going to even begin to contemplate identifying SEQ ID NO: 4 variants that retain ITIM signaling activity.

Moreover, the prior art of Davis et al (7,317,087) teaches that a polypeptide differing from SEQ ID NO: 4 only in the first 7 residues of its N-terminal signal sequence, FcRH6, is part of a larger family of polypeptides with homology to the classical Fc receptors, e.g.., FcγRII (see Davis cols. 1 and 2). Indeed, pos-filing date art demonstrates that FcRH6 is capable of binding MHC class II, i.e., it binds a ligand unlike any other ligand bound by any other NKIR (see Schreeder et al., J. Immunol. 2010;185;23-27, page 26, concluding remarks, cited herewith).

The instant claims and essentially call for trial and error by the skilled artisan to begin discovering how to make the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.

As put forth in Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), "[i]f mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Similarly, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc. v. Novo Nordisk, 42 USPQ 2d 1001,(CAFC 1997), the court held: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". Further, "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 14, 21-24, 26, 28-30, 43, 44, 46 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Vas-Cath, Inc., v. Mahurkar, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116.

The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, such as its ability to mediate ITIM signaling activity, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. In re Bell, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). In re Deuel, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995).

In the instant case, the specification provides insufficient direction or guidance concerning the relationship between the structure of SEQ ID NO: 4 and its ability to mediate ITIM signaling activity to demonstrate possession of the claimed genus of variant polypeptides.

The instant claims encompass in their breadth a nearly infinite number of derivatives, and yet the specification lacks direction/guidance regarding which structural features are required in order to provide activity.

The problem of predicting protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the

sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function ... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

Furthermore, in the absence of this guidance or direction the skilled artisan would not consider applicant to be in possession of the claimed genus of polypeptides because the skilled artisan recognizes that even seemingly minor changes made without guidance or direction as to the relationship between the structure of SEQ ID NO: 4 and its ability to bind and be dimerized by some unknown ligand can dramatically affect mediate ITIM signaling.

Applicant has not described the claimed invention sufficiently to show they had possession of the claimed genus of polypeptides.

Sufficient description to show possession of such a genus "may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004).

Moreover, according to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, MPEP 2163 II.A.3a.ii.

Applicant is directed to the Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/
Primary Examiner, Art Unit 1644